

**REMARKS/ARGUMENTS****Telephone Interview and Applicants' Statement of the Substance of the Interview**

Applicants wish to thank the Examiner for conducting a telephone interview with Applicants' attorney, Diane P. Tso (Reg. No. 46,012) on September 23, 2010 and for forwarding the Interview Summary dated September 27, 2010. Applicants believe that the Examiner's summary of the interview is accurate.

Applicants also acknowledge with appreciation a follow-up conversation between Examiner Fronda and Applicants' attorney on January 10, 2011 with regard to the submission by Applicants of additional evidence in support of the patentability of the pending claims.

**Claim Disposition**

Claims 1-3 and 5-29 are currently pending, claim 4 having been previously cancelled. Claims 8-25 and 27-29 are currently withdrawn as directed to non-elected subject matter. Claims 1-3, 5-7 and 26 are under examination.

Applicants acknowledge the withdrawal by the Examiner of the previous rejection of claims 1-3, 5-7 and 26 under 35 U.S.C. § 112, second paragraph and 35 U.S.C § 102(b) in view of the amendments and arguments filed by Applicants on March 1, 2010.

Claims 1-3, 5-7 and 26 currently stand rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking enablement. Specifically, the Examiner has alleged that the specification, while being enabling for a method for the demonstration of the occurrence of an apoptotic event in a cell comprising detecting the presence of the GFP fused to the

N-terminal of Bax comprising the amino acid sequence of SEQ ID NO:2, it does not reasonably provide enablement for other embodiments. The Examiner has further alleged that the specification does not provide guidance, prediction, and/or working examples regarding demonstration of any other molecular event other than an apoptotic event, thus it would require undue experimentation for one skilled in the art to make and/or use the invention commensurate in scope with the claims.

In a sincere attempt to facilitate prosecution of the instant application, and further to the conversation between the Examiner and Applicants' attorney of January 10, 2011, Applicants respectfully submit herein for the Examiner's consideration a copy of *Florea et al., Biochimica et Biophysica Acta* 1783 (2008) 1551-1560 (hereafter "*Florea et al.*") co-authored by inventor Francois Ichas. This reference describes the development of an efficient and quantitative high content assay for gamma-secretase activity in live cells, directed towards either APP or Notch, designed to identify endogenous regulators, as well as new candidate inhibitor compounds, by means of high-throughput screening and which is based on the methods of the instant invention. Specifically, as described in detail in *Florea et al.*, experimental methods using plasma membrane permeabilization and marker proteins with a fluorescent fragment such as described in the present invention were successfully used to demonstrate gamma-secretase activity in living cells (see, e.g., *Florea et al.* at Figure 1). Thus, Applicants submit that the experiments described in *Florea et al.* show that the methods of the present invention may be used without undue experimentation to demonstrate the occurrence of a molecular event other than apoptosis.

*Florea et al.* clearly relies on the guidance provided in the instant specification and what was well known to one of skill in the art at the time the application was filed. Indeed, the authors expressly teach that

[o]ur strategy consisted in the generation of retention probes capable to convert positional signals into intensity responses. The method is based on the differential retention of fluorescent recombinant proteins following plasma membrane permeabilization and is suitable for detecting a variety of molecular events, such as proteolytic activities and changes in intracellular compartmentalization [31].

*Florea et al.* at page 1558. Applicants respectfully draw the Examiner's attention to the fact that Reference 31 cited at the end of this passage is Applicants' French Patent No. FR2857098 and WO 2005/012913, and to which the instant application claims priority.

Applicants submit that the teachings of *Florea et al.* provide sufficient facts and evidence in support of the scope of the claimed invention, and are believed appropriate to submit to the USPTO for consideration by the Examiner at this time in view of the Examiner's outstanding rejections of the claimed invention under 35 U.S.C. § 112, first paragraph.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. Moreover, rejoinder of the withdrawn claims is respectfully requested.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

A Petition for a three-month extension of time is being filed concurrently herewith. If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefore.

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Respectfully submitted,  
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